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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Parent Art Unit: 1655
Susumu ARIMORI et al.	Parent Examiner: Betty J. Forman
Serial No: Not Assigned	
Filed: Herewith	
For: PHOTO-INDUCED ELECTRON TRANSFER FLUORESCENT SENSOR MOLECULES	

PRELIMINARY AMENDMENT

BOX PATENT APPLICATION
U.S. Patent and Trademark Office
P.O. Box 2327
Arlington, VA 22202

Dear Sir:

Prior to the first Office Action in the present application, please enter and consider the following amendments and remarks:

IN THE SPECIFICATION:

Please replace the text of the last paragraph on page 4 and the first paragraph on page 5 with the following text:

In the above formula, Fl is a fluorophore, N is a nitrogen atom, Bd1 and Bd2 are independently selected binding groups, Sp is an aliphatic spacer, and An is an anchor group for attaching the sensor to solid substrates. n, m, x, and y are integers, where n = 1 or 2, m = 1 or 2, and y =1 or 2. The binding groups are capable of binding an analyte molecule to form a stable 1:1 complex. Examples of

binding groups include, but are not limited to, boronic acid, crown ether, and aza-crown ether, such as 1,4,7,10,13-Pentaoxa-16-aza-cyclooctadecane (aza 18-crown-6) and 1,4,7,13-tetraoxa-10-aza-cyclohexadecane (aza 15-crown-5). In a preferred embodiment, the Bd1 is R1-B(OH)2 and Bd2 is R2-B(OH)2. R1 and R2 are aliphatic or aromatic functional groups selected independently from each other and B is a boron atom.

Please replace the text of the first full paragraph on page 8 with the following text:

In the present invention, the binding groups may be any functional groups, as long as they provide the desired specific binding of the analyte to the sensor with a formation of 1:1 complex. The binding groups are preferably electron deficient groups. The electron deficiency governs the shift of the unshared electron pair from the nitrogen atoms to the binding group when specifically binding the analyte. Examples of the acceptable binding groups include, but are not limited to, boronic acid, crown ether, and aza-crown ether, such as 1,4,7,10,13-Pentaoxa-16-aza-cyclooctadecane (aza 18-crown-6) and 1,4,7,13-tetraoxa-10-aza-cyclohexadecane (aza 15-crown-5). Examples of analytes that may be identified by utilizing sensors of the present invention include, but are not limited to, saccharides, amino saccharides, and carbonyl saccharides.

IN THE CLAIMS:

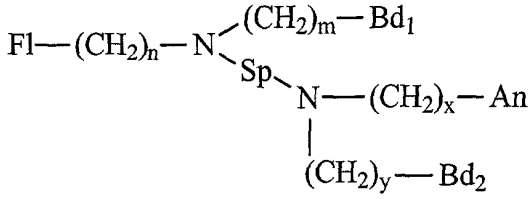
Please cancel claims 1-21 without prejudice.

Please replace the text of claim 33 with the following text:

33. (Amended) A method of labeling solid substrates, comprising:

(a) providing a solid substrate;

(b) providing the modular fluorescence sensor having the following general formula:



wherein:

Fl is a fluorophore;

N is a nitrogen atom;

B_{d1} and B_{d2} are independently selected binding groups, wherein the binding groups are capable of binding an analyte molecule to form a stable 1:1 complex;

Sp is an aliphatic spacer;

n, m, x, and y are integers, where n = 1 or 2, m = 1 or 2, and y =1 or 2; and

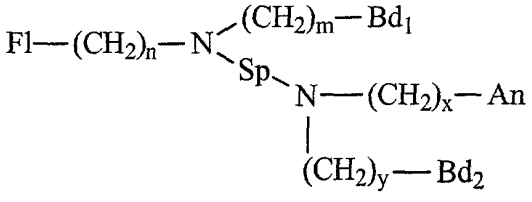
An is an anchor group capable of being attached to the solid substrate;

(c) reacting the sensor with the solid substrate under a condition sufficient to attach the sensor to the substrate.

Please add new claims 40-60 as follows:

40. (New) A method for detecting an analyte contained in a sample comprising the steps of:

(a) providing a modular fluorescence sensor having the following general formula:



wherein:

Fl is a fluorophore;

N is a nitrogen atom;

B_{d1} and B_{d2} are independently selected binding groups, wherein the binding groups are capable of binding the analyte molecule to form a stable 1:1 complex;

Sp is an aliphatic spacer;

An is an anchor group for attaching the sensor to a solid substrate; and

n, m, x, and y are integers, where n = 1 or 2, m = 1 or 2, and y =1 or 2;

(b) contacting the sensor with the sample whereby the sensor binds the analyte and generates a detectable analyte signal that is responsive to the analyte concentration in the sample;

(c) detecting the generated analyte signal; and

(d) determining the concentration of the analyte contained in the sample.

41. (New) The method of claim 40, wherein the analyte is selected from the group consisting of saccharides, amino saccharides, and carbonyl saccharides.

42. (New) The method of claim 41, wherein the Sp comprises six carbon atoms and the analyte is glucose.

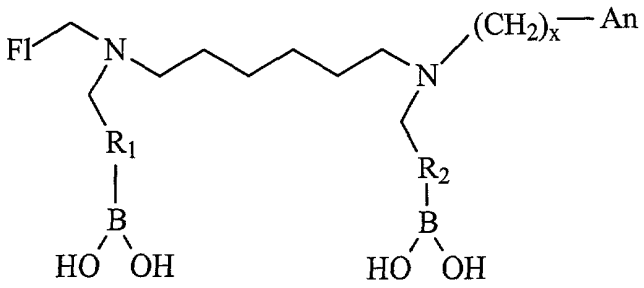
43. (New) The method of claim 40, wherein Fl is selected from the group consisting of naphtyl, anthryl, pyrenyl, phenanthryl, and perylene.

44. (New) The method of claim 40, wherein B_{d1} is R_1-$B(OH)_2$ and B_{d2} is R_2-$B(OH)_2$, wherein R_1 and R_2 are aliphatic or aromatic functional groups selected independently from each other and B is a boron atom.

45. (New) The method of claim 44, wherein R_1 and R_2 selected from the group consisting of: methyl, ethyl, propyl, butyl, phenyl, methoxy, ethoxy, butoxy, and phenoxy groups.

46. (New) The method of claim 40, wherein An comprises methyl or phenyl.

47. (New) The method of claim 40, wherein the modular fluorescence sensor has the following general formula:



wherein:

B is a boron atom; and

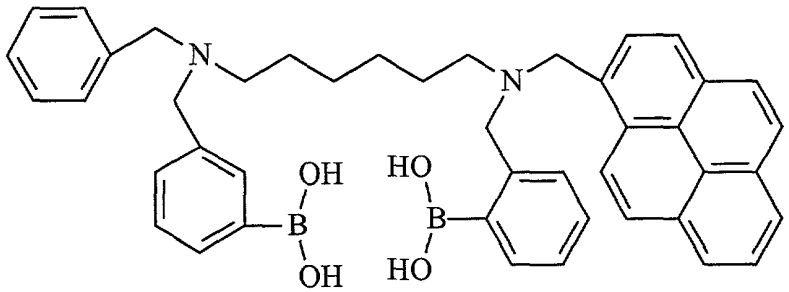
R_1 and R_2 are aliphatic or aromatic functional groups which allow covalent binding of an analyte to the hydroxyl groups forming a stable 1:1 complex, wherein R_1 and R_2 are selected independently from each other.

48. (New) The method of claim 47, wherein Fl is selected from the group consisting of naphtyl, anthryl, pyrenyl, phenanthryl, and perylene.

49. (New) The sensor of claim 47, wherein R_1 and R_2 are independently selected from the group consisting of: methyl, ethyl, propyl, butyl, phenyl, methoxy, ethoxy, butoxy, and phenoxy groups.

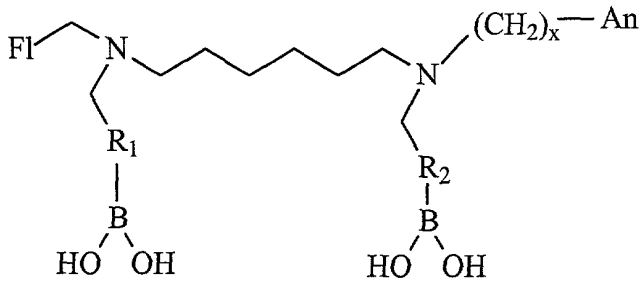
50. (New) The method of claim 47, wherein the analyte is glucose.

51. (New) The method of claim 40, wherein the analyte is glucose and the modular fluorescence sensor has the following general formula:



52. (New) A method for detecting glucose contained in a sample comprising the steps of:

(a) providing a modular fluorescence sensor having the following general formula:



wherein:

Fl is a fluorophore;

N is a nitrogen atom;

B is a boron atom;

R_1 and R_2 are aliphatic or aromatic functional groups which allow covalent binding of an analyte to the hydroxyl groups forming a stable 1:1 complex, wherein R_1 and R_2 are selected independently from each other;

An is an anchor group for attaching the sensor to a solid substrate; and

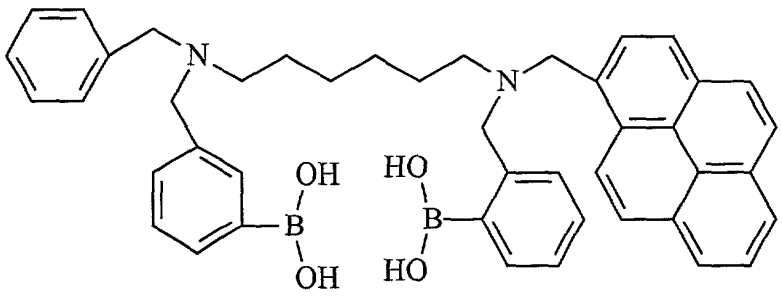
x is an integer.

(b) contacting the sensor with the sample whereby the sensor binds the analyte and generates a detectable analyte signal that is responsive to the analyte concentration in the sample;

(c) detecting the generated analyte signal; and

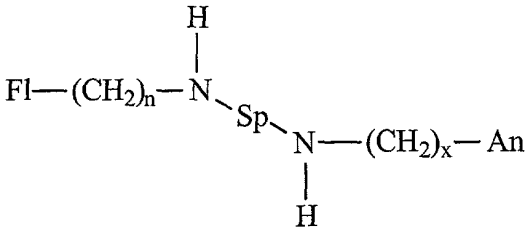
(d) determining the concentration of the analyte contained in the sample.

53. (New) The method of claim 52, wherein the analyte is glucose and the modular fluorescence sensor has the following formula:



54. (New) A method for detecting an analyte contained in a sample comprising the steps of:

(a) forming an asymmetric compound of the following general formula:



wherein:

Fl is a fluorophore;

N is a nitrogen atom and H is a hydrogen atom;

Sp is an aliphatic spacer;

An is an anchor group for attaching the sensor to a solid substrate; and

n = 1 or 2, and x is any integer; and

(b) replacing hydrogen atoms with B_{d1} and B_{d2} groups to form a modular fluorescence sensor, wherein B_{d1} and B_{d2} are independently selected binding groups capable of binding an analyte molecule to form a stable 1:1 complex.

(c) contacting the sensor with the sample whereby the sensor binds the analyte and generates a detectable analyte signal that is responsive to the analyte concentration in the sample;

(d) detecting the generated analyte signal; and

(e) determining the concentration of the analyte contained in the sample.

55. The method of claim 54, wherein Fl is selected from the group consisting of naphtyl, anthryl, pyrenyl, phenanthryl, and perylenyl.

56. The method of claim 54, wherein B_{d1} is R_1-$B(OH)_2$ and B_{d2} is R_2-$B(OH)_2$, wherein R_1 and R_2 are aliphatic or aromatic functional groups selected independently from each other, and B is a boron atom.

57. The method of claim 56, wherein R_1 and R_2 selected from the group consisting of: methyl, ethyl, propyl, butyl, phenyl, methoxy, ethoxy, butoxy, and phenoxy groups.

58. The method of claim 54, wherein the step of replacing of hydrogen atoms comprises adding orthobromomethyl phenylboronic acid.

59. The method of claim 54, wherein Sp is a straight-chain alkane.

60. The method of claim 54, wherein *An* comprises an organic functionality.

REMARKS

Minor changes are made to the specification. Claims 1-21 are canceled without prejudice. Claim 33 amended; marked up version of the amended claim is attached hereto pursuant to 37 C.F.R. § 1.121(c)(ii). New claims 40-60 are added. No new matter is introduced. The support for claims 40-60 can be found on page 8, lines 1-15; page 10, lines 5-26; and page 15, lines 5-21. Claims 22-60 are pending in the application.

Entry of this amendment and examination on the merits of this application is respectfully requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles, California telephone number 213-337-6700 to discuss the steps necessary for placing the application in condition for allowance.

Respectfully submitted,

HOGAN & HARTSON L.L.P.

Date: January 17, 2002

By: ______________________
Wei-Ning Yang
Registration No. 38,690
Attorney for Applicant(s)

500 South Grand Avenue, Suite 1900
Los Angeles, California 90071
Phone: 213-337-6700
Fax: 213-337-6701

Version with markings to show changes made:

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Please replace the text of the first full paragraph on page 8 with the following text:

In the present invention, the binding groups may be any functional groups, as long as they provide the desired specific binding of the analyte to the sensor with a formation of 1:1 complex. The binding groups are preferably electron deficient groups. The electron deficiency governs the shift of the unshared electron pair from the nitrogen atoms to the binding group when specifically binding the analyte. Examples of the acceptable binding groups include, but are not limited to, [one] boronic acid, [one] crown ether, and aza-crown [ethers] ether, such as 1,4,7,10,13-Pentaoxa-16-aza-cyclooctadecane (aza 18-crown-6) and 1,4,7,13-tetraoxa-10-aza-cyclohexadecane (aza 15-crown-5). Examples of analytes that may be identified by

utilizing sensors of the present invention include, but are not limited to, saccharides, amino saccharides, and carbonyl saccharides.

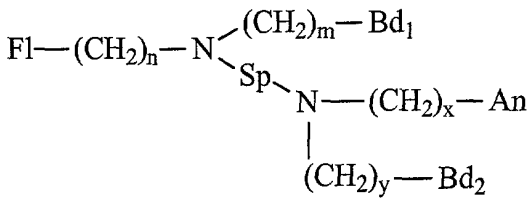
IN THE CLAIMS:

Please replace the text of claim 33 with the following text:

33. (Amended) A method of labeling solid substrates, comprising:

(a) providing a solid substrate;

(b) providing the modular fluorescence sensor [of claim 1,] having the following general formula:



wherein:

Fl is a fluorophore;

N is a nitrogen atom;

B_{d1} and B_{d2} are independently selected binding groups, wherein the binding groups are capable of binding an analyte molecule to form a stable 1:1 complex;

Sp is an aliphatic spacer;

n, m, x, and y are integers, where n = 1 or 2, m = 1 or 2, and y =1 or 2; and

An is an anchor group capable of being attached to the solid substrate;

(c) reacting the sensor with the solid substrate under a condition sufficient to attach the sensor to the substrate.